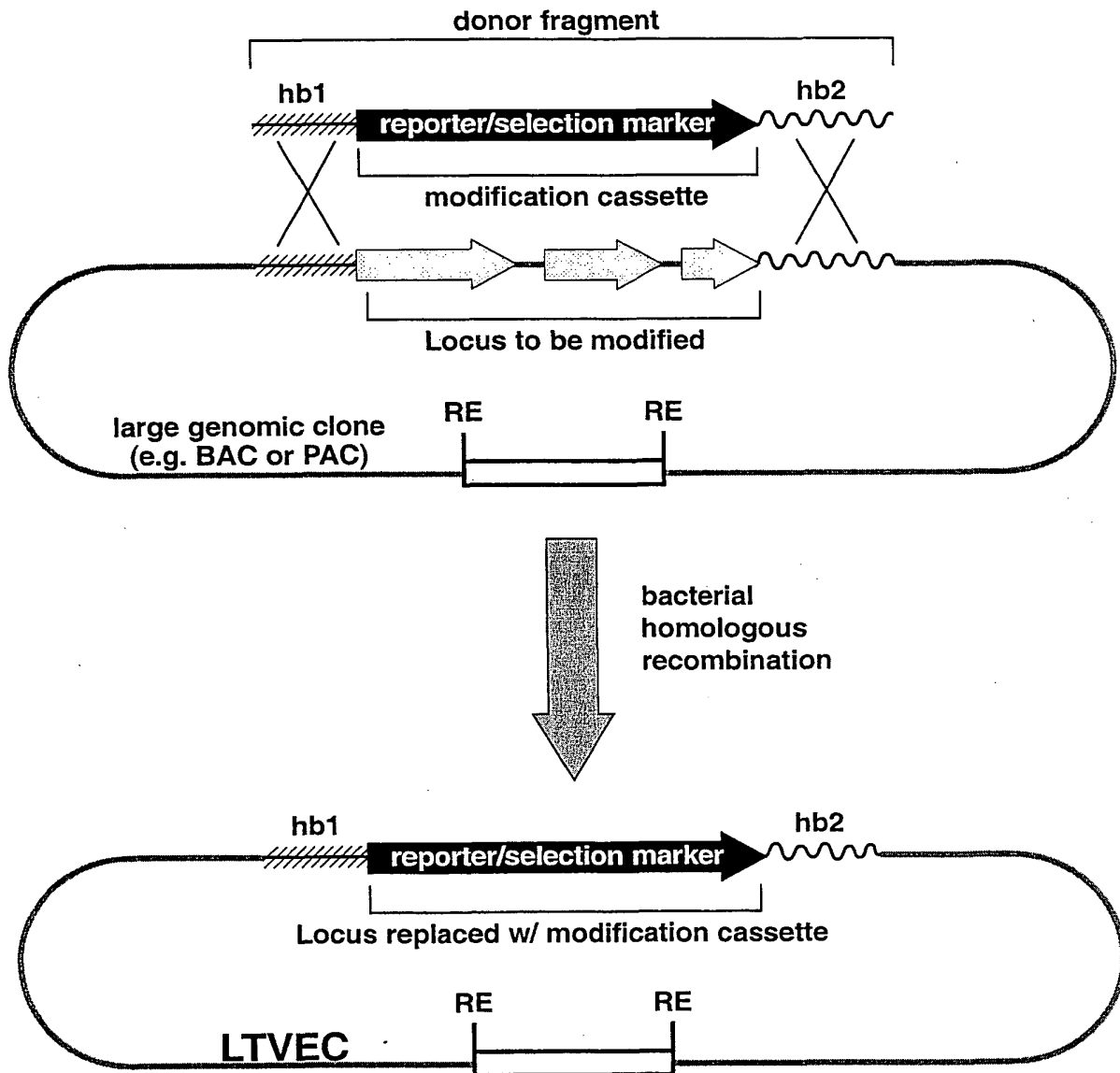
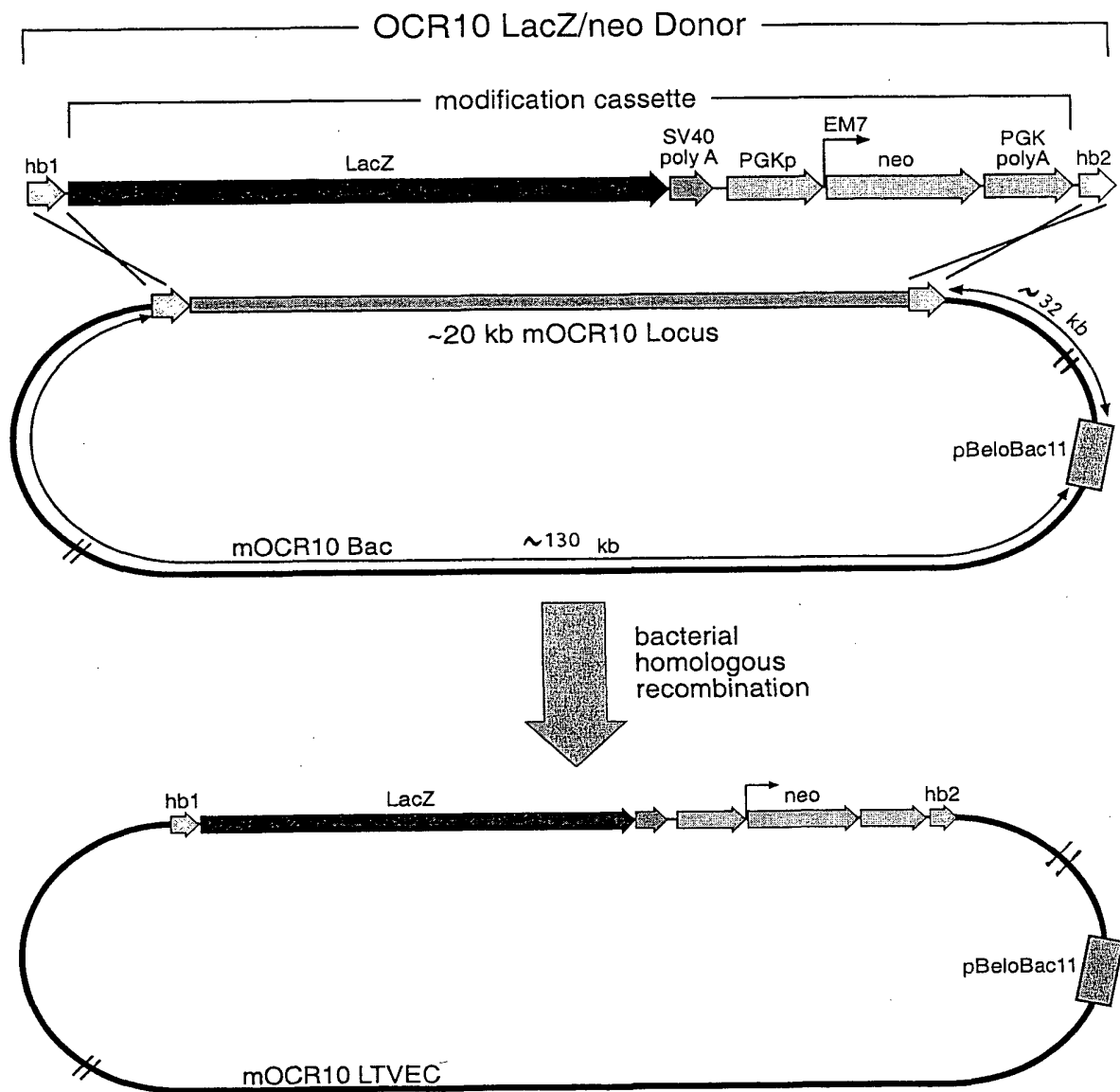


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Figure 1



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 Figure 2



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FIGURE 3A

10 20 30 40 50 60
CCCCGGGCTT CCTGTTCTAA TAAGAATACC TCCTAGGTCC CCCATGGGCT AACCTCATCT
GGGGCCCGAA GGACAAGATT ATTCTTATGG AGGATCCAGG GGGTACCCGA TTGGAGTAGA

70 80 90 100 110 120
TTGGTACTCA ACAGGGGTCT TCTTTATGAG CTTCGGACCA GCTCTTTTGA TGTGGCAGGG
AACCATGAGT TGTCCCCAGA AGAAATACTC GAAGCCTGGT CGAGAAACT ACACCGTCCC

130 140 150 160 170 180
ACTGACCCTG GGTGGGGAAG CCACTCAGTG CATGACCCCA GCTGGTTCAC CACATATACC
TGACTGGGAC CCACCCCTTC GGTGAGTCAC GTACTGGGGT CGACCAAGTG GTGTATATGG

190 200 210 220 230
ACATACTTTT CTTGCAGGTC TGGGACACAG C ATG CCC CGG GGC CCA GTG GCT GCC
TGTATGAAAA GAACGTCCAG ACCCTGTGTC G TAC GGG GCC CCG GGT CAC CGA CGG
Met Pro Arg Gly Pro Val Ala Ala>

240 250 260 270 280
TTA CTC CTG CTG ATT CTC CAT GGA GCT TGG AGC TGC CTG GAC CTC ACT
AAT GAG GAC GAC TAA GAG GTA CCT CGA ACC TCG ACG GAC CTG GAG TGA
Leu Leu Leu Leu Ile Leu His Gly Ala Trp Ser Cys Leu Asp Leu Thr>

290 300 310 320 330
TGC TAC ACT GAC TAC CTC TGG ACC ATC ACC TGT GTC CTG GAG ACA CGG
ACG ATG TGA CTG ATG GAG ACC TGG TAG TGG ACA CAG GAC CTC TGT GCC
Cys Tyr Thr Asp Tyr Leu Trp Thr Ile Thr Cys Val Leu Glu Thr Arg>

340 350 360 370
AGC CCC AAC CCC AGC ATA CTC AGT CTC ACC TGG CAA GAT GAA TAT GAG
TCG GGG TTG GGG TCG TAT GAG TCA GAG TGG ACC GTT CTA CTT ATA CTC
Ser Pro Asn Pro Ser Ile Leu Ser Leu Thr Trp Gln Asp Glu Tyr Glu>

380 390 400 410 420
GAA CTT CAG GAC CAA GAG ACC TTC TGC AGC CTA CAC AAG TCT GGC CAC
CTT GAA GTC CTG GTT CTC TGG AAG ACG TCG GAT GTG TTC AGA CCG GTG
Glu Leu Gln Asp Gln Glu Thr Phe Cys Ser Leu His Lys Ser Gly His>

430 440 450 460 470
AAC ACC ACA CAT ATA TGG TAC ACG TGC CAT ATG CGC TTG TCT CAA TTC
TTG TGG TGT GTA TAT ACC ATG TGC ACG GTA TAC GCG AAC AGA GTT AAG
Asn Thr Thr His Ile Trp Tyr Thr Cys His Met Arg Leu Ser Gln Phe>

480 490 500 510 520
CTG TCC GAT GAA GTT TTC ATT GTC AAC GTG ACG GAC CAG TCT GGC AAC
GAC AGG CTA CTT CAA AAG TAA CAG TTG CAC TGC CTG GTC AGA CCG TTG
Leu Ser Asp Glu Val Phe Ile Val Asn Val Thr Asp Gln Ser Gly Asn>

530 540 550 560 570
AAC TCC CAA GAG TGT GGC AGC TTT GTC CTG GCT GAG AGC ATC AAG CCA
TTG AGG GTT CTC ACA CCG TCG AAA CAG GAC CGA CTC TCG TAG TTC GGT
Asn Ser Gln Glu Cys Gly Ser Phe Val Leu Ala Glu Ser Ile Lys Pro>

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FIGURE 3B

	580		590		600		610								
GCT	CCC	CCC	TTG	AAC	GTG	ACT	GTG	GCC	TTC	TCA	GGA	CGC	TAT	GAT	ATC
CGA	GGG	GGG	AAC	TTG	CAC	TGA	CAC	CGG	AAG	AGT	CCT	GCG	ATA	CTA	TAG
Ala	Pro	Pro	Leu	Asn	Val	Thr	Val	Ala	Phe	Ser	Gly	Arg	Tyr	Asp	Ile>
620		630		640		650		660							
TCC	TGG	GAC	TCA	GCT	TAT	GAC	GAA	CCC	TCC	AAC	TAC	GTG	CTG	AGA	GGC
AGG	ACC	CTG	AGT	CGA	ATA	CTG	CTT	GGG	AGG	TTG	ATG	CAC	GAC	TCT	CCG
Ser	Trp	Asp	Ser	Ala	Tyr	Asp	Glu	Pro	Ser	Asn	Tyr	Val	Leu	Arg	Gly>
670		680		690		700		710							
AAG	CTA	CAA	TAT	GAG	CTG	CAG	TAT	CGG	AAC	CTC	AGA	GAC	CCC	TAT	GCT
TTC	GAT	GTT	ATA	CTC	GAC	GTC	ATA	GCC	TTG	GAG	TCT	CTG	GGG	ATA	CGA
Lys	Leu	Gln	Tyr	Glu	Leu	Gln	Tyr	Arg	Asn	Leu	Arg	Asp	Pro	Tyr	Ala>
720		730		740		750		760							
GTG	AGG	CCG	GTG	ACC	AAG	CTG	ATC	TCA	GTG	GAC	TCA	AGA	AAC	GTC	TCT
CAC	TCC	GGC	CAC	TGG	TTC	GAC	TAG	AGT	CAC	CTG	AGT	TCT	TTG	CAG	AGA
Val	Arg	Pro	Val	Thr	Lys	Leu	Ile	Ser	Val	Asp	Ser	Arg	Asn	Val	Ser>
770		780		790		800		810							
CTT	CTC	CCT	GAA	GAG	ATC	CAC	AAA	GAT	TCT	AGC	TAC	CAG	CTG	CAG	ATG
GAA	GAG	GGA	CTT	CTC	AAG	GTG	TTT	CTA	AGA	TCG	ATG	GTC	GAC	GTC	TAC
Leu	Leu	Pro	Glu	Glu	Phe	His	Lys	Asp	Ser	Ser	Tyr	Gln	Leu	Gln	Met>
820		830		840		850									
CGG	GCA	GCG	CCT	CAG	CCA	GGC	ACT	TCA	TTC	AGG	GGG	ACC	TGG	AGT	GAG
GCC	CGT	CGC	GGA	GTC	GGT	CCG	TGA	AGT	AAG	TCC	CCC	TGG	ACC	TCA	CTC
Arg	Ala	Ala	Pro	Gln	Pro	Gly	Thr	Ser	Phe	Arg	Gly	Thr	Trp	Ser	Glu>
860		870		880		890		900							
TGG	AGT	GAC	CCC	GTC	ATC	TTT	CAG	ACC	CAG	GCT	GGG	GAG	CCC	GAG	GCA
ACC	TCA	CTG	GGG	CAG	TAG	AAA	GTC	TGG	GTC	CGA	CCC	CTC	GGG	CTC	CGT
Trp	Ser	Asp	Pro	Val	Ile	Phe	Gln	Thr	Gln	Ala	Gly	Glu	Pro	Glu	Ala>
910		920		930		940		950							
GGC	TGG	GAC	CCT	CAC	ATG	CTG	CTG	CTC	CTG	GCT	GTC	TTG	ATC	ATT	GTC
CCG	ACC	CTG	GGA	GTG	TAC	GAC	GAC	GAG	GAC	CGA	CAG	AAC	TAG	TAA	CAG
Gly	Trp	Asp	Pro	His	Met	Leu	Leu	Leu	Leu	Ala	Val	Leu	Ile	Ile	Val>
960		970		980		990		1000							
CTG	GTT	TTC	ATG	GGT	CTG	AAG	ATC	CAC	CTG	CCT	TGG	AGG	CTA	TGG	AAA
GAC	CAA	AAG	TAC	CCA	GAC	TTC	TAG	GTG	GAC	GGA	ACC	TCC	GAT	ACC	TTT
Leu	Val	Phe	Met	Gly	Leu	Lys	Ile	His	Leu	Pro	Trp	Arg	Leu	Trp	Lys>
1010		1020		1030		1040		1050							
AAG	ATA	TGG	GCA	CCA	GTG	CCC	ACC	CCT	GAG	AGT	TTC	TTC	CAG	CCC	CTG
TTC	TAT	ACC	CGT	GGT	CAC	GGG	TGG	GGA	CTC	TCA	AAG	AAG	GTC	GGG	GAC
Lys	Ile	Trp	Ala	Pro	Val	Pro	Thr	Pro	Glu	Ser	Phe	Phe	Gln	Pro	Leu>

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Att. Docket No. REG 780D
Inventors: Andrew J. Murphy, et al.
Title: METHODS OF MODIFYING
EUKARYOTIC CELLS

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FIGURE 3C

1060	1070	1080	1090
TAC AGG GAG CAC AGC	GGG AAC TTC	AAG AAA TGG GTT	AAT ACC CCT TTC
ATG TCC CTC GTG TCG	CCC TTG AAG TTC	TTT ACC CAA TTA	TGG GGA AAG
Tyr Arg Glu His Ser	Gly Asn Phe Lys	Lys Trp Val Asn	Thr Pro Phe>
1100	1110	1120	1130
ACG GCC TCC AGC ATA	GAG TTG GTG CCA	CAG AGT TCC ACA	ACA ACA TCA
TGC CGG AGG TCG TAT	CTC AAC CAC GGT	GTC TCA AGG TGT	TGT TGT AGT
Thr Ala Ser Ser Ile	Glu Leu Val Pro	Gln Ser Ser Thr	Thr Thr Ser>
1150	1160	1170	1180
GCC TTA CAT CTG TCA	TTG TAT CCA GCC	AAG GAG AAG AAG	TTC CCG GGG
CGG AAT GTA GAC AGT	AAC ATA GGT CGG	TTC CTC TTC AAG	GGC CCC
Ala Leu His Leu Ser	Leu Tyr Pro Ala	Lys Glu Lys Lys	Phe Pro Gly>
1200	1210	1220	1230
CTG CCG GGT CTG GAA	GAG CAA CTG GAG	TGT GAT GGA ATG	TCT GAG CCT
GAC GGC CCA GAC CTT	CTC GTT GAC CTC	ACA CTA CCT TAC	AGA CTC GGA
Leu Pro Gly Leu Glu	Glu Gln Leu Glu	Cys Asp Gly Met	Ser Glu Pro>
1250	1260	1270	1280
GGT CAC TGG TGC ATA	ATC CCC TTG GCA	GCT GGC CAA GCG	GTC TCA GCC
CCA GTG ACC ACG TAT	TAG GGG AAC CGT	CGA CCG GTT CGC	CAG AGT CCG
Gly His Trp Cys Ile	Ile Pro Leu Ala	Ala Gly Gln Ala	Val Ser Ala>
1300	1310	1320	1330
TAC AGT GAG GAG AGA	GAC CCG CCA TAT	GGT CTG GTG TCC	ATT GAC ACA
ATG TCA CTC CTC TCT	CTG GCC GGT ATA	CCA GAC CAC AGG	TAA CTG TGT
Tyr Ser Glu Glu Arg	Asp Arg Pro Tyr	Gly Leu Val Ser	Ile Asp Thr>
1340	1350	1360	1370
GTG ACT GTG GGA GAT	GCA GAG GGC CTG	TGT GTC TGG CCC	TGT AGC TGT
CAC TGA CAC CCT CTA	CGT CTC CCG GAC	ACA CAG ACC GGG	ACA TCG ACA
Val Thr Val Gly Asp	Ala Glu Gly Leu	Cys Val Trp Pro	Cys Ser Cys>
1390	1400	1410	1420
GAG GAT GAT GGC TAT	CCA GCC ATG AAC	CTG GAT GCT GGC	AGA GAG TCT
CTC CTA CTA CCG ATA	GGT CCG TAC TTG	GAC CTA CGA CCG	TCT CTC AGA
Glu Asp Asp Gly Tyr	Pro Ala Met Asn	Leu Asp Ala Gly	Arg Glu Ser>
1440	1450	1460	1470
GGT CCT AAT TCA GAG	GAT CTG CTC TTG	GTC ACA GAC CCT	GCT TTT CTG
CCA GGA TTA AGT CTC	CTA GAC GAG AAC	CAG TGT CTG GGA	CGA AAA GAC
Gly Pro Asn Ser Glu	Asp Leu Leu Leu	Val Thr Asp Pro	Ala Phe Leu>
1490	1500	1510	1520
TCT TGT GGC TGT GTC	TCA GGT AGT GGT	CTC AGG CTT GGG	GGC TCC CCA
AGA ACA CCG ACA CAG	AGT CCA TCA CCA	GAG TCC GAA CCC	CCG AGG GGT
Ser Cys Gly Cys Val	Ser Gly Ser Gly	Leu Arg Leu Gly	Gly Ser Pro>

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Figure 3D

1540 1550 1560 1570
GGC AGC CTA CTG GAC AGG TTG AGG CTG TCA TTT GCA AAG GAA GGG GAC
CCG TCG GAT GAC CTG TCC AAC TCC GAC AGT AAA CGT TTC CTT CCC CTG
Gly Ser Leu Leu Asp Arg Leu Arg Leu Ser Phe Ala Lys Glu Gly Asp>

1580 1590 1600 1610 1620
TGG ACA GCA GAC CCA ACC TGG AGA ACT GGG TCC CCA GGA GGG GGC TCT
ACC TGT CGT CTG GGT TGG ACC TCT TGA CCC AGG GGT CCT CCC CCG AGA
Trp Thr Ala Asp Pro Thr Trp Arg Thr Gly Ser Pro Gly Gly Gly Ser>

1630 1640 1650 1660 1670
GAG AGT GAA GCA GGT TCC CCC CCT GGT CTG GAC ATG GAC ACA TTT GAC
CTC TCA CTT CGT CCA AGG GGG GGA CCA GAC CTG TAC CTG TGT AAA CTG
Glu Ser Glu Ala Gly Ser Pro Pro Gly Leu Asp Met Asp Thr Phe Asp>

1680 1690 1700 1710 1720
AGT GGC TTT GCA GGT TCA GAC TGT GGC AGC CCC GTG GAG ACT GAT GAA
TCA CCG AAA CGT CCA AGT CTG ACA CCG TCG GGG CAC CTC TGA CTA CTT
Ser Gly Phe Ala Gly Ser Asp Cys Gly Ser Pro Val Glu Thr Asp Glu>

1730 1740 1750 1760 1770
GGA CCC CCT CGA AGC TAT CTC CGC CAG TGG GTG GTC AGG ACC CCT CCA
CCT GGG GGA GCT TCG ATA GAG GCG GTC ACC CAC CAG TCC TGG GGA GGT
Gly Pro Pro Arg Ser Tyr Leu Arg Gln Trp Val Val Arg Thr Pro Pro>

1780 1790 1800
CCT GTG GAC AGT GGA GCC CAG AGC AGC TAG
GGA CAC CTG TCA CCT CGG GTC TCG TCG ATC
Pro Val Asp Ser Gly Ala Gln Ser Ser ***>

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Figure 4A Human Ig heavy chain locus (total length $\approx 1\text{Mb}$, not drawn to scale):

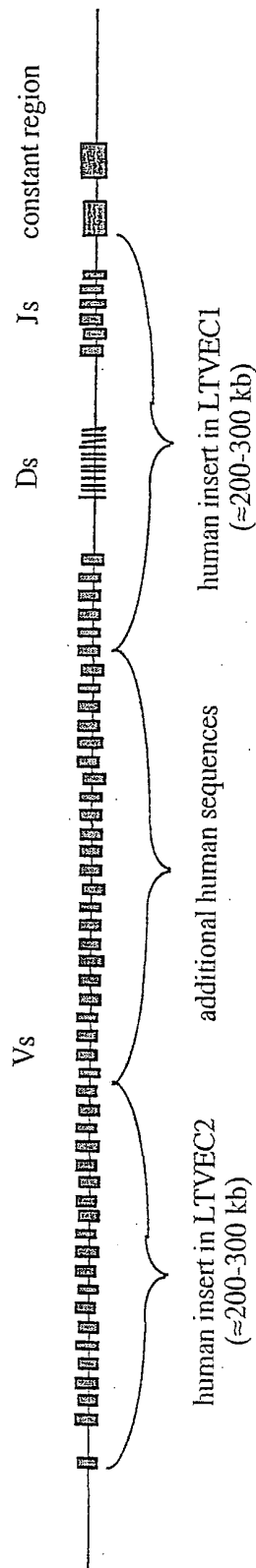


Figure 4B Mouse Ig heavy chain locus (total length $\approx 1\text{Mb}$, not drawn to scale):

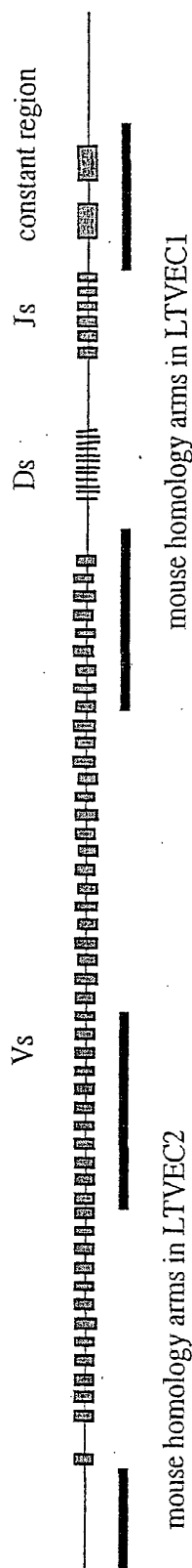


Figure 4C LTV2C2:

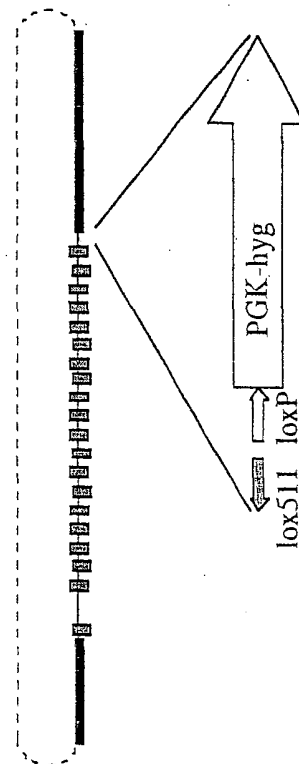


Figure 4d LTV2C1:

